PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference LEVO-RENAL	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/FI2004/000002	International filing date *(day/month/year)* 02.01.2004	Priority date *(day/month/year)* 03.01.2003
International Patent Classification (IPC) or national classification and IPC A61K31/50, A61P13/12		
Applicant ORION CORPORATION et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.07.2004	31.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Telephone No. +31 70 340- Fletcher, A.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI2004/000002

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-7 as originally filed

   Claims, Numbers

   1-4 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 3,4

because:

☒ the said international application, or the said claims Nos. 3,4 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. 1,11,15-18

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-4
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	see separate sheet
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III.

Claims 3,4 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

No International Preliminary Examination will be carried out in respect of subject matter which is not covered by the search report (Rule 66.1 (e) PCT).

Re Item V.

1 The following documents are referred to in this communication:

D1 : DATABASE WPI Section Ch, Week 199314
Derwent Publications Ltd., London, GB; Class B03, AN 1993-111711
XP002283338 &; JP 04 368328 A (TEIKOKU HORMONE MFG CO LTD) 21 December 1992 (1992-12-21)

D2 : EP 0 565 546 A (ORION YHTYMAE OY) 20 October 1993 (1993-10-20)

D3 : PAGEL P S ET AL: "PHARMACOLOGY OF LEVOSIMENDAN: A NEW MYOFILAMENT CALCIUM SENSITIZER" CARDIOVASCULAR DRUG REVIEWS, NEVA PRESS, BRANFORD, CT, US, vol. 14, no. 3, 1996, pages 286-316, XP008030915 ISSN: 0897-5957

D4 : PAGEL P S HETTRICK D A ET AL: "INFLUENCE OF LEVOSIMENDAN PIMOBENDAN, AND MILRINONE ON THE REGIONAL DISTRIBUTION OF CARDIAC OUTPUT IN ANAESTHETIZED DOGS" 1996, BRITISH JOURNAL OF PHARMACOLOGY, BASINGSTOKE, HANTS, GB, PAGE(S) 609-615 , XP002901958 ISSN: 0007-1188

2 Document D1, which is considered to represent the most relevant state of the art, discloses (see the abstract) the use 6-(4-acetylamino-phenyl)-4,5-dihydro-5-methyl -3(2H)-pyridazinone salt(s) for enhancing contractive force of the heart and remedying the failure, without increasing of oxygen consumption of the heart muscle. It also has action of reducing the refluxing flow of the vein and expanding the peripheral vessel, being effective against chronic renal failure: the compound is structurally very close to levosimendan
From this, the subject-matter of independent claim 1 differs in that levosimendan

has a hydrazonopropanedinitrile derivative in exchange of a acetylamino group.

2.1 The subject-matter of claim 1 is therefore novel (Article 33(2) PCT)
The problem to be solved by the present invention may be regarded as to provide a altenative compound for the treatment of renal failure.

2.2 The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons: There is no incentive in the prior art for exchanging the acetylamino group by a hydrazonopropanedinitrile.

2.3 Claims 2-4 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

3 Documents D2-D4, which are considered to represent the most relevant state of the art, disclose (see the passages cited in the search report): the use of levosimendan in relation to the treatment of congestive heart failure.
From this, the subject-matter of independent claim 1 differs in that it solves the problem of treating renal failure.

3.1 The subject-matter of claim 1 is therefore novel (Article 33(2) PCT)
The problem to be solved by the present invention may be regarded as to provide for a novel use for levosimendan.

3.2 The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons: There is no incentive in the prior art for using levosimendan in relation to the treatment of renal failure.

3.3 Claims 2-4 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to novelty and inventive step.